absorbance at about 330 nm, with a suitable spectrophotometer, using the solvent as the blank. Calculate the quantity, in mg, of prazosin ($C_{19}H_{21}N_5O_4$) in the Capsule taken by the formula:

$$(383.40/419.86)(0.001DC)(A_U / A_S)$$

in which 383.40 and 419.86 are the molecular weights of prazosin and prazosin hydrochloride, respectively; *D* is the dilution factor for the Capsule contents; *C* is the concentration, in µg per mL, of USP Prazosin Hydrochloride RS, calculated on the anhydrous basis, in the Standard solution; and A_U and A_S are the absorbances of the solution from the Capsule contents and the Standard solution, respectively.

Assay—

Mobile phase, *Chromatographic system*, and *Procedure*—Proceed as directed in the *Assay* under *Prazosin Hydrochloride*.

Acid–methanol solution—To 300 mL of water in a 1000-mL volumetric flask, add 0.85 mL of hydrochloric acid, dilute with methanol to volume, and mix. Transfer 300 mL of this solution to a 500-mL volumetric flask, dilute with methanol to volume, and mix.

Standard preparation—Prepare a solution of USP Prazosin Hydrochloride RS in *Acid–methanol solution* having a known concentration of about 0.2 mg per mL. Pipet 5 mL of this solution into a 100-mL volumetric flask, add 45.0 mL of *Acid–methanol solution*, dilute with methanol to volume, and mix.

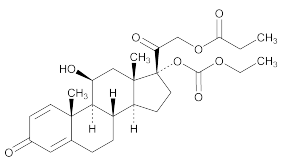
Assay preparation—Remove, as completely as possible, the contents of not less than 20 Capsules, and weigh. Transfer a quantity of the contents, accurately weighed, equivalent to about 1 mg of prazosin hydrochloride, to a glass-stoppered flask containing 50.0 mL of *Acid–methanol solution*, and shake by mechanical means for 30 minutes. Place the flask in an ultrasonic bath for 30 minutes, cool to room temperature, and filter the contents through a membrane filter (5 µm or finer porosity). Transfer 25.0 mL of the filtrate to a 50-mL volumetric flask, dilute with methanol to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Prazosin Hydrochloride*. Calculate the quantity, in mg, of prazosin ($C_{19}H_{21}N_5O_4$) in the portion of the contents of Capsules taken by the formula:

$$(383.40/419.86)(0.1C)(r_U / r_S)$$

in which 383.40 and 419.86 are the molecular weights of prazosin and prazosin hydrochloride, respectively; *C* is the concentration, in µg per mL, of USP Prazosin Hydrochloride RS, calculated on the anhydrous basis, in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Prednicarbate



$C_{27}H_{36}O_8$ 488.57

(1) Pregna-1,4-diene-3,20-dione, 17-[(ethoxycarbonyl)oxy]-11-hydroxy-21-(1-oxopropoxy)-, (11*β*)-.

(2) 11*β*,17,21-Trihydroxypregna-1,4-diene-3,20-dione 17-(ethyl carbonate) 21-propionate [73771-04-7].

» Prednicarbate contains not less than 97.0 percent and not more than 102.0 percent of $C_{27}H_{36}O_8$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed, light-resistant containers.

USP Reference standards ⟨11⟩**—**
USP Prednicarbate RS
USP Prednicarbate Related Compound A RS
1,2-Dihydroprednicarbate.

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Specific rotation ⟨781S⟩**:** between +60° and +66°.

Test solution: 10 mg per mL, in alcohol.

Loss on drying ⟨731⟩**—**Dry it at 105° for 6 hours: it loses not more than 0.5% of its weight.

Chromatographic purity—

Mobile phase, Resolution solution, and *Chromatographic system*—Prepare as directed in the *Assay.*

Test solution—Use the *Assay preparation*.

Diluted test solution—Transfer 1 mL of the *Test solution* to a 200-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Procedure—Separately inject equal volumes (about 20 µL) of the *Test solution* and the *Diluted test solution* into the chromatograph, record the chromatograms, and measure the response for the prednicarbate peak obtained from the *Diluted test solution.* Obtain from the *Test solution* the peak responses for prednicarbate related compound A and for all peaks other than prednicarbate. Continue the chromatography for twice the retention time of prednicarbate. Calculate the percentage of the related compound and all the impurities in the portion of Prednicarbate taken by the formula:

$$0.5(r_T / r_{DT})$$

in which r_T is the peak response for each individual impurity peak obtained from the *Test solution;* and r_{DT} is the peak response of the main peak in the chromatogram of the *Diluted test solution:* not more than 1.0% of prednicarbate related compound A is found; not more than 0.5% of any other individual impurity is found, with the exception of the main peak and the peak corresponding to prednicarbate related compound A; and not more than 2.0% of total impurities is found. Disregard any peak (0.0125%) with an area less than 0.025 times the area of the main peak in the chromatogram obtained from the *Diluted test solution*.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of water and acetonitrile (60:50). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Resolution solution—Dissolve suitable quantities of USP Prednicarbate Related Compound A RS and Prednicarbate in *Mobile phase* to obtain a solution containing about 3 µg of each per mL. [NOTE—Prepare all solutions just prior to use.]

Standard preparation—Dissolve an accurately weighed quantity of USP Prednicarbate RS in *Mobile phase,* and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.6 mg per mL.

Assay preparation—Transfer about 30 mg of Prednicarbate, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 243-nm detector and a 4-mm × 12.5-cm column that contains packing L1. The flow rate is about 0.7 mL per minute. Chromatograph the *Resolution solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.1 for prednicarbate related compound A and 1.0 for prednicarbate; and the

resolution, *R,* between prednicarbate and prednicarbate related compound A is not less than 3.0.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the prednicarbate peaks. Continue the chromatography for twice the retention time of prednicarbate. Calculate the quantity, in mg, of $C_{27}H_{36}0_8$ in the portion of Prednicarbate taken by the formula:

$$50C(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Prednicarbate RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Prednicarbate Cream

» Prednicarbate Cream contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of prednicarbate ($C_{27}H_{36}O_8$). It may contain a suitable preservative.

Packaging and storage—Preserve in tight, light-resistant containers, and store at controlled room temperature.

USP Reference standards ⟨11⟩**—**
USP Prednicarbate RS
USP Prednicarbate Related Compound A RS
1,2-Dihydroprednicarbate.
USP Prednicarbate Related Compound B RS
Prednisolone-17-ethylcarbonate.
USP Prednicarbate Related Compound C RS
Prednisolone-21-propionate.

Identification—The retention time of the prednicarbate peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Consistency—At room temperature, a string of Cream having a length of 2 cm retains its shape on a glass plate for at least 10 minutes. It can be spread easily and has no visible lumps.

Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩**—**It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The total aerobic bacterial count does not exceed 100 cfu per g.

Minimum fill ⟨755⟩**:** meets the requirements.

pH ⟨791⟩**:** between 3.5 and 5.0, in a solution prepared in the following manner. Add 15 mL of boiling water to 3.5 g of Cream in a 50-mL centrifuge tube, and shake vigorously until an emulsion is formed. Loosen the cap, and place in a steam bath for 5 minutes. Centrifuge the hot solution. After cooling to room temperature, collect the lower aqueous solution in a glass tube, and determine the pH.

Related compounds—

Solution A, Solution B, Mobile phase, Solution 1, Solution 2, and *Resolution solution*—Prepare as directed in the *Assay.*

Standard stock solution—Prepare as directed for *Standard stock preparation* in the *Assay.*

Standard solution—Prepare as directed for *Standard preparation* in the *Assay.*

System sensitivity solution—Dilute 1.0 mL of the *Standard solution* with dehydrated alcohol to 50.0 mL. Dilute 1.0 mL of the solution thus obtained with *Solution A* to 20.0 mL.

Test solution—Prepare as directed for the *Assay preparation.*

Chromatographic system—Proceed as directed in the *Assay*. Chromatograph the *System sensitivity solution:* the signal-to-noise ratio is not less than 3. Chromatograph the *Resolution solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.57 for prednicarbate related compound B, 0.64 for prednicarbate related compound C, 1.0 for prednicarbate, and 1.04 for prednicarbate related compound A.

Procedure—Inject a volume (about 60 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure the peak responses. Calculate the percentage of each related compound and unknown impurity in the portion of Cream taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the peak response for each individual impurity obtained from the *Test solution,* and r_s is the sum of the peak responses obtained from the *Test solution:* not more than 2.0% of prednicarbate related compound B and not more than 2.0% of prednicarbate related compound C is found; not more than 0.5% of any individual related compound is found; and not more than 5.0% of total related compounds is found.

Assay—

Solution A—Prepare a 0.01 M solution of monobasic potassium phosphate in water.

Solution B—Prepare a mixture of acetonitrile and dehydrated alcohol (2:1).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard stock preparation—Dissolve an accurately weighed quantity of USP Prednicarbate RS in dehydrated alcohol, and dilute quantitatively, and stepwise if necessary, with dehydrated alcohol to obtain a solution having a known concentration of 0.3 mg per mL.

Standard preparation—Transfer 10.0 mL of the *Standard stock preparation* to a 100-mL volumetric flask, add 15 mL of tetrahydrofuran and 30 mL of *Solution B,* and dilute with *Solution A* to volume.

Assay preparation—Transfer an accurately weighed quantity of Cream, equivalent to about 3.0 mg of prednicarbate, to a 100-mL volumetric flask. Add 15 mL of tetrahydrofuran, shake vigorously, and allow to stand in an ultrasonic bath until the sample has dissolved. Add 20 mL of dehydrated alcohol, and shake vigorously. Add 20 mL of acetonitrile, and shake vigorously. Immediately dilute with *Solution A* to volume, and shake vigorously. Allow to stand in an ice bath for at least 15 minutes. Shake the samples vigorously, and pass through a folded paper filter. Pass the filtrate through a membrane filter of 0.45-µm porosity.

Solution 1—Prepare a solution containing 0.3 mg per mL each of USP Prednicarbate Related Compound B RS and USP Prednicarbate Related Compound C RS in dehydrated alcohol.

Solution 2—Transfer about 15 mg of USP Prednicarbate Related Compound A RS, accurately weighed, to a 50-mL volumetric flask; add 1.0 mL of *Solution 1,* and dilute with dehydrated alcohol to volume.

Resolution solution—Transfer 10.0 mL of the *Standard preparation* to a volumetric flask; add 1.0 mL of *Solution 2,* 1 mL of tetrahydrofuran, and 2 mL of acetonitrile; and dilute with *Solution A* to 20.0 mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 243-nm detector and a 4.0-mm × 25-cm column that contains 5-µm packing L1. The column temperature is maintained at 40°. The flow rate is about 1 mL per minute. The chromatograph is programmed as follows.